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This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-76. (Canceled)

77. (New) A gene-targeted, rodent heterozygous for a human mutation of the presentiin-1 (PS-1) gene and heterozygous for an amyloid precursor protein (APP) gene of said rodent having a human FAD Swedish mutation, and a humanized Aβ nucleotide sequence.

78. (New) A gene-targeted, rodent homozygous for a human mutation of the presenilin-1 (PS-1) gene and homozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation, and a humanized A β nucleotide sequence.

79. (New) A gene-targeted rodent homozygous for a human mutation of the presentilin-1 (PS-1) gene and heterozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation and a humanized Aβ nucleotide sequence.

- 80. (New) A gene-targeted rodent heterozygous for a human mutation of the presenilin-1 (PS-1) gene and homozygous for an amyloid precursor protein (APP) gene of said mammal having a human FAD Swedish mutation and a humanized Aβ nucleotide sequence.
 - 81. (New) The rodent of claim 77 wherein said mutation of said PS-1 gene is P264L.
 - 82. (New) The rodent of claim 78 wherein said mutation of said PS-1 gene is P264L.
 - 83. (New) The rodent of claim 79 wherein said mutation of said PS-1 gene is P264L.
 - 84. (New) The rodent of claim 80 wherein said mutation of said PS-1 gene is P264L.

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85. (New) The rodent of claim 77 wherein said rodent is a mouse.

86. (New) The rodent of claim 78 wherein said rodent is a mouse.

87. (New) The rodent of claim 79 wherein said rodent is a mouse.

88. (New) The rodent of claim 80 wherein said rodent is a mouse.

89. (New) Generational offspring of the rodent of claim 77 wherein said mutant PS-1 gene is expressed.

90. (New) Generational offspring of the rodent of claim 78 wherein said mutant PS-1 gene is expressed.

- 91. (New) Generational offspring of the rodent of claim 79 wherein said mutant PS-1 gene is expressed.
- 92. (New) Generational offspring of the rodent of claim 80 wherein said mutant PS-1 gene is expressed.
- 93. (New) A method for screening chemical compounds for the ability to decrease *in* vivo levels of $A\beta$ peptide, said method comprising the steps of:
 - a) administering said chemical compound to the rodent of claim 77; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.
- 94. (New) A method for screening chemical compounds for the ability to decrease *in* vivo levels of A β peptide, said method comprising the steps of:
 - a) administering said chemical compound to the rodent of claim 78; and
 - b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent,

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wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.

95. (New) A method for screening chemical compounds for the ability to decrease *in vivo* levels of Aβ peptide, said method comprising the steps of:

- a) administering said chemical compound to the rodent of claim 79; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.

96. (New) A method for screening chemical compounds for the ability to decrease *in vivo* levels of Aβ peptide, said method comprising the steps of:

- a) administering said chemical compound to the rodent of claim 80; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.
- 97. (New) A method for screening chemical compounds for the ability to decrease *in* vivo levels of $A\beta$ peptide, said method comprising the steps of:
 - a) administering said chemical compound to the rodent of claim 89; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.
- 98. (New) A method for screening chemical compounds for the ability to decrease *in vivo* levels of Aβ peptide, said method comprising the steps of:
 - a) administering said chemical compound to the rodent of claim 90; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.

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99. (New) A method for screening chemical compounds for the ability to decrease *in vivo* levels of Aβ peptide, said method comprising the steps of:

- a) administering said chemical compound to the rodent of claim 91; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.
- 100. (New) A method for screening chemical compounds for the ability to decrease *in* vivo levels of $A\beta$ peptide, said method comprising the steps of:
 - a) administering said chemical compound to the rodent of claim 92; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a chemical compound that has the ability to decrease *in vivo* levels of said $A\beta$ peptide.
- 101. (New) The method of claim 93 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 102. (New) The method of claim 94 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 103. (New) The method of claim 95 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 104. (New) The method of claim 96 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 105. (New) The method of claim 97 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 106. (New) The method of claim 98 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

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107. (New) The method of claim 99 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.

- 108. (New) The method of claim 100 wherein said tissue sample is selected from the group consisting of brain tissue, non-brain tissue and body fluids.
- 109. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 77; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 110. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 78; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 111. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 79; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 112. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 80; and

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b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

- 113. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 89; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 114. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 90; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 115. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 91; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.
- 116. (New) A method for identifying a compound for treating Alzheimer's disease comprising the steps of:
 - a) administering a compound to the rodent of claim 92; and
- b) measuring the amount of $A\beta$ peptide in a tissue sample from said rodent, wherein a decrease in the amount of $A\beta$ peptide in said tissue sample is indicative of a compound that can be used to treat Alzheimer's disease.

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117. (New) The method of claim 109 wherein said tissue sample is selected from the

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group consisting of brain tissue, non-brain tissue and body fluids.

118. (New) The method of claim 110 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

119. (New) The method of claim 111 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

120. (New) The method of claim 112 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

121. (New) The method of claim 113 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

122. (New) The method of claim 114 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

123. (New) The method of claim 115 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

124. (New) The method of claim 116 wherein said tissue sample is selected from the

group consisting of brain tissue, non-brain tissue and body fluids.

125. (New) The rodent of claim 81 wherein codon 264 of the PS-1 gene is changed

from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.

126. (New) The rodent of claim 125 wherein codon 264 of the PS-1 gene is changed

from CCG to CTT.

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127. (New) The rodent of claim 81 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

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- 128. (New) The rodent of claim 82 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.
- 129. (New) The rodent of claim 128 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.
- 130. (New) The rodent of claim 82 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.
- 131. (New) The rodent of claim 83 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.
- 132. (New) The rodent of claim 131 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.
- 133. (New) The rodent of claim 83 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.
- 134. (New) The rodent of claim 84 wherein codon 264 of the PS-1 gene is changed from CCG to CTT, CTC, CTA, CTG, TTA, or TTG.
- 135. (New) The rodent of claim 134 wherein codon 264 of the PS-1 gene is changed from CCG to CTT.
- 136. (New) The rodent of claim 84 wherein codon 265 of the PS-1 gene is changed from AAA to AAG.

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137. (New) The rodent of claim 77 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I, M146L (A \Rightarrow T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A \Rightarrow C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W,S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow T with S290C), a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow A with S290C), a \triangle exon 9 Finn 4,555 basepair deletion, a \triangle intron 4 splice donor consensus sequence G deletion, a C \Rightarrow T mutation at position -48 in the 5' promoter, a C \Rightarrow G mutation at position -280 in the 5' promoter, or a A \Rightarrow G mutation at position -2818 in the 5' promoter.

138. (New) The rodent of claim 78 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I, M146L (A \Rightarrow T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A \Rightarrow C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W,S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow T with S290C), a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow A with S290C), a \triangle exon 9 Finn 4,555 basepair deletion, a \triangle intron 4 splice donor consensus sequence G deletion, a C \Rightarrow T mutation at position -48 in the 5' promoter, a C \Rightarrow G mutation at position -280 in the 5' promoter, or a A \Rightarrow G mutation at position -2818 in the 5' promoter.

139. (New) The rodent of claim 79 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I, M146L (A⇒T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A⇒C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, Page 11 of 13

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P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W,S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a Δ exon 9 splice acceptor site deletion mutation (G \Rightarrow T with S290C), a Δ exon 9 splice acceptor site deletion mutation (G \Rightarrow A with S290C), a Δ exon 9 Finn 4,555 basepair deletion, a Δ intron 4 splice donor consensus sequence G deletion, a C \Rightarrow T mutation at position -48 in the 5' promoter, a C \Rightarrow G mutation at position -280 in the 5' promoter, or a A \Rightarrow G mutation at position -2818 in the 5' promoter.

140. (New) The rodent of claim 80 wherein said human mutation of the PS-1 gene is A79V, V82L, V96F, Y115C, E120D, E120K, M139I, M139T, M139V, I143F, I143T, M146I, M146L (A \Rightarrow T), H163Y, G209V, A231T, A231V, M233T, L235P, L250S, A260V, L262F, C263R, P264L, P267S, R269H, R278T, E280A, E280G, A285V, E318G, G378E, G384A, L392V, M146L (A \Rightarrow C), M146V, H163R, I213T, L286V, A246E, Y115H, T116N, P117L, L171P, E123L, N135D, C410Y, A426P, P436S, M139K, T147I, W165C, L173W,S390I, L166R, S169L, P436Q, S169P, E184D, G209R, L219P, M233L, A409T, E273A, L282R, G378A, N405S, A409T, L424R, a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow T with S290C), a \triangle exon 9 splice acceptor site deletion mutation (G \Rightarrow A with S290C), a \triangle exon 9 Finn 4,555 basepair deletion, a \triangle intron 4 splice donor consensus sequence G deletion, a C \Rightarrow T mutation at position -48 in the 5' promoter, a C \Rightarrow G mutation at position -280 in the 5' promoter, or a A \Rightarrow G mutation at position -2818 in the 5' promoter.